

# Alerts, Notices, and Case Reports

## Urticarial Skin Lesions and Polymyositis Due to Lymphocytic Vasculitis

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URTICARIA is a common disorder in the general population. Approximately 20% of people have acute urticaria at least once during their lifetime.<sup>1</sup> The differential diagnosis of urticaria can be extensive. Urticariogenic factors can be grouped into several categories, including physical agents, contactants, ingestants, inhalants, infections, systemic diseases, and psychogenic factors.<sup>2</sup> Within the category of systemic diseases, an important possibility is vasculitis.

When vasculitis causes an urticarial skin eruption, the histopathologic study of a biopsy specimen usually reveals leukocytoclastic vasculitis.<sup>3</sup> Other types of vasculitis, however, are occasionally documented by histopathologic studies of biopsy specimens taken from active skin lesions. For example, hypocomplementemic urticarial vasculitis syndrome (HUVS) may develop in patients with high titers of C1q precipitins in the serum.<sup>4</sup> We present here the findings in an adult with long-standing urticarial skin lesions resulting not from leukocytoclastic vasculitis or HUVS, but from a lymphocytic vasculitis.

### Report of a Case

The patient, a 49-year-old woman, was referred for the evaluation of urticarial skin lesions of three years' duration. The lesions typically began in the evening and were accompanied by a burning sensation rather than pruritus. The lesions generally lasted 48 to 96 hours and healed with hyperpigmentation. After an asymptomatic interval of four to five days, another cycle would occur. Her condition had steadily worsened during the year before the evaluation. Although antihistamines did not relieve her skin discomfort, oral corticosteroids at high doses were effective. Ten months before the evaluation, daily treatment with prednisone, 10 mg taken each morning, was initiated. This treatment reduced the occurrence of the skin lesions but did not eliminate them.

Her medical history revealed that 14 years before the evaluation, she was admitted to hospital for treatment of a right middle lobe pneumonia that failed to clear with antibiotic therapy. Lymph node biopsy specimens showed noncaseating granulomas consistent with sarcoidosis. She received treatment with prednisone for four years and had not had any reactivation of sarcoidosis after the prednisone was discontinued. Two years before the evaluation, after a vaginal hysterectomy, treatment with estrogen and calcium supplements was initiated. She had no known allergies. She denied alcohol or drug abuse. She was employed as an insurance agent and had no known exposures to occupational toxins or allergens. She smoked six to eight cigarettes daily for 30 years. Her family history was remarkable for atopic disorders. The review of systems revealed fatigue, curved fingernails, and weakness of her arms and legs, particularly proximally.

On physical examination, the patient's skin had slightly raised, red, 5-mm<sup>2</sup>, irregularly shaped lesions on her head that blanched with pressure. Her anterior cervical lymph nodes were mildly enlarged. Her nails were moderately clubbed. The strength of extremity muscles, particularly proximal muscles, was mildly reduced. The remainder of the physical examination showed no abnormalities.

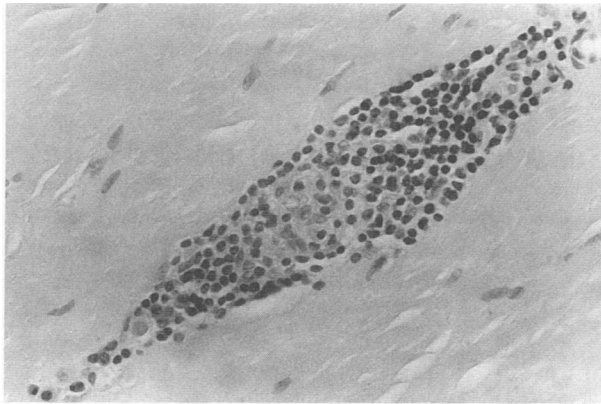
The results of initial laboratory studies, including a complete blood count, platelet count, urinalysis, syphilis serologic test, antinuclear antibodies, complement profile, circulating immune complex assays, hepatitis virus (A, B, and C) serologic tests, cryoglobulins, and serum angiotensin I-converting enzyme level, were within normal limits. The erythrocyte sedimentation rate was 35 mm per hour (normal, 0 to 20). Serum chemistry levels revealed modest elevations of alanine aminotransferase (103 U per liter; normal, 0 to 55) and lactate dehydrogenase (450 U per liter; normal, 0 to 270). There were notable elevations of creatine kinase (4,945 U per liter; normal, 45 to 235) and aldolase levels (51 U per liter; normal, 1 to 8). Creatine kinase isoenzyme analysis documented skeletal muscle as the site of origin of the elevated serum creatine kinase level.

Based on the clinical and laboratory findings, skin and muscle biopsies were done. Both biopsy specimens showed lymphocytic vasculitis (Figure 1). Specifically, there was a lymphocytic inflammatory infiltrate centered around and in blood vessels with fibrinoid changes in the vessel walls. Some infiltrate extended into the surrounding connective tissue. There was little infiltrate in muscle fibers. Immunofluorescence stains of skin tissue and several special stains of muscle tissue were uniformly normal. Additional laboratory tests, including phenotyping lymphocytes for surface membrane immunoglobulin, CD19, CD20, CD3, CD4, CD8, CD16, CD56, HLA-DR, and CD10 plus CD5 to exclude a lymphoma; Jo-1 antibody titers; and serologic tests for toxoplasmosis,

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**Figure 1.**—The vessel wall has a lymphocytic infiltrate that extends also into the perimysial connective tissue (hematoxylin and eosin stain, original magnification  $\times 200$ ).

human immunodeficiency virus, and Lyme disease were negative.

The final diagnosis was idiopathic lymphocytic vasculitis with secondary urticarial skin lesions and polymyositis. The prednisone dose was increased to 40 mg by mouth each morning. Although the skin lesions vanished quickly, the fatigue, myalgias, and weakness resolved slowly during the first eight weeks of treatment. Various laboratory values decreased to the normal range over three months (Table 1). The daily prednisone dose was tapered by 5 mg per month; even after the dose was reduced to 11 mg daily, the vasculitis continued to be quiescent by clinical measurements, although the erythrocyte sedimentation rate increased slightly.

### Discussion

Although many diseases produce skin discomfort, urticaria is distinguished by pruritic wheals that resolve

**TABLE 2.**—Clinical Conditions Associated With Lymphocytic Vasculitis

<b>Conditions with known cause</b>
Adverse drug reactions
Necrobiosis lipoidica diabetorum
Nodular scabies
Insect bites
Viral infections
Rickettsial infections
Spirochetal infections—syphilis
Lepromatous leprosy
<b>Conditions without known cause</b>
Pigmented purpuric eruptions
Lymphomatoid granulomatosis
Angiocentric immunoproliferative lesion
Wegener's granulomatosis
Sarcoidosis
Behçet's disease
Systemic lupus erythematosus
Sjögren's syndrome
$\alpha_1$ -Antitrypsin deficiency panniculitis
<b>Dermatologic reaction patterns</b>
Urticaria
Hypocomplementemic urticarial vasculitis syndrome
Erythema multiforme
Pityriasis lichenoides et varioliformis acuta
Lymphomatoid papulosis
Erythema perstans
Granuloma annulare
Pyoderma gangrenosum

**TABLE 1.**—Response of Laboratory Values to Oral Steroid Therapy

Treatment Week	Laboratory Values		Prednisone Dose, mg each AM
	Creatine Kinase, U/liter*	Erythrocyte Sedimentation Rate, mm/hr†	
0 .....	4,945	35	3
1 .....	4,613	--	40
5 .....	2,134	--	40
6 .....	1,158	--	40
7 .....	465	10	40
10 .....	93	23	35
15 .....	30	20	35
18 .....	13	34	30
29 .....	26	29	25
33 .....	26	13	20
46 .....	21	27	15
54 .....	27	24	14
62 .....	28	46	13
78 .....	33	39	11

\*Normal, 45 to 235 U per liter.

†Normal, 0 to 20 mm per hour.

completely. Lesions may be referred to as urticarial if they have characteristics such as persistence beyond 24 hours, burning, pain, or sequelae (such as hyperpigmentation or scarring). The differential diagnosis of urticarial skin lesions frequently focuses on vasculitis (including HUVS) and autoimmune diseases, but includes thyroid disorders and viral infections (such as hepatitis B). When clinicians evaluate urticarial lesions to diagnose or exclude vasculitis, they should obtain a biopsy of skin.

Vasculitis, like many other systemic diseases, frequently has diverse manifestations. Therefore, it can be included in the differential diagnosis of almost any sign or symptom. Microscopic studies of a vasculitic skin lesion demonstrate leukocytes infiltrating the walls of affected vessels. In most vasculitic syndromes, these cells are predominantly neutrophils and the complement system is activated. This activation can be detected in the blood as hypocomplementemia, circulating immune complexes, and on microscopy, fibrinoid degradation. In a few patients, however, the number of lymphocytes exceeds the number of neutrophils, and there is no evidence of complement activation.<sup>5</sup> In these patients, the initial diagnosis is lymphocytic vasculitis.

In the case reported here, the pathologic process identified histologically as lymphocytic vasculitis was

responsible for the urticarial skin eruption that was the presenting symptom. Further clinical evaluation showed that the lymphocytic vasculitis also was responsible for the polymyositis that had been identified on physical examination and confirmed by serum enzyme levels. The cause of polymyositis, an inflammatory process affecting symmetrical skeletal muscle groups, is identified only in some patients.<sup>6</sup> Causative agents include adverse reactions to ingestants, autoimmune diseases, malignant neoplasms, sarcoidosis,<sup>7,9</sup> and vasculitis.<sup>10</sup> Although our patient had well-documented sarcoidosis in the past, our clinical, serologic, and histologic evaluation failed to provide any evidence of reactivation of her previous disorder. Thus, to our knowledge, this is the first reported case of a lymphocytic vasculitis producing both polymyositis and urticarial skin lesions.

The differential diagnosis of a lymphocytic vasculitis includes autoimmune diseases, infections, malignant neoplasms, adverse reactions to ingestants, and inflammatory disorders of unknown origin (Table 2).<sup>11-15</sup> When the cause of lymphocytic vasculitis is known, the underlying cause should be removed or treated. Patients such as the one reported here with an unidentified etiologic factor frequently require treatment with anti-inflammatory medication, which may include corticosteroids, azathioprine, and cyclophosphamide. When these medications are used, the lymphocytic vasculitis is usually well controlled.

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## Impotence Related to Anabolic Steroid Use in a Body Builder Response to Clomiphene Citrate

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THE RECREATIONAL USE of anabolic steroids has become commonplace among athletes.<sup>1,2</sup> Exercise enthusiasts frequently subscribe to information from such sources as the "Underground Steroid Handbook"<sup>3</sup> and self-design illicit drug therapy, including the use of human chorionic gonadotropin (hCG), clomiphene citrate (Clomid), and tamoxifen citrate, to counter the side effects of gynecomastia and reduced testicular volume. Despite this apparent drug sophistication, not only can these persons have a psychological dependence on the anabolic steroids,<sup>4,5</sup> but hypogonadotropic hypogonadism that lasts for months<sup>6,7</sup> to years<sup>8</sup> may also develop.

The case presented here illustrates the degree of drug knowledge among body builders, the psychosocial dependence on these drugs, and the potential of clomiphene<sup>9</sup> in treating the disorder of pituitary-gonadal failure in such persons.

#### Report of a Case

The patient, a 29-year-old man, had impotence and decreased libido for a year. He is a college student and a competitive body builder who had used anabolic steroids for eight months (January to August 1992), alternating 16-week cycles of testosterone cypionate (Depo-Testosterone), 1,500 to 1,800 mg per week, and oxymetholone (Anadrol), 560 mg per week. After stopping the use of these drugs in August 1992, he was impotent with no spontaneous erections and had diminished libido. He completed a self-selected four-week trial of human chorionic gonadotropin (hCG) in September 1992 without any change in libido and no improvement in potency. The dose of hCG is unknown, and the patient denied any previous use of the drug. He was advised by colleagues to take a course of clomiphene or await the spontaneous return of sexual

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